New Diagnostic and Treatment Techniques in Cryptococcal Meningitis

POSITIVE CEREBROSPINAL FLUID latex agglutination of cryptococcal antigen was found in patients with chronic meningitis not diagnosable by India ink preparations or cultures of the cerebrospinal fluid. To date, the latex agglutination technique appears more sensitive than the complement fixation test for the detection of cryptococcal antigen in the cerebrospinal fluid. A false positive reaction may appear in the serum latex agglutination cryptococcal antigen test due to the presence of circulating rheumatoid factor in the serum, but this does not occur in testing the cerebrospinal fluid. The Communicable Disease Center in Atlanta has been able to perform the cerebrospinal fluid latex agglutination cryptococcal antigen test on patients suspected of cryptococcal meningitis.

Before the introduction of amphotericin B in 1956, cryptococcal meningitis was almost invariably fatal. Now, in approximately two-thirds of patients this agent can eradicate the organism from the spinal fluid. Initially, 1 mg of the drug is diluted in 5 percent glucose in water and administered intravenously. The dosage is rapidly increased to deliver 1.0 to 1.5 mg per kg of body weight per day, although it is unusual to exceed 50 mg a day. Side effects include headaches, chills, fever, and vomiting in addition to potentially non-reversible renal damage which is directly related to the total dosage. Frequent monitoring of the urine, hemoglobin, serum creatinine, and blood urea nitrogen is mandatory. A therapeutic end-point is rarely sharply delineated and treatment is generally continued to deliver a total of 2,000 to 2,500 mg in six weeks to four months. Intrathecal therapy is reserved for the critically ill or patients in relapse.

Since the first report of its effectiveness in cryptococcal meningitis in 1967, 5-flurocytosine (5-FC), has been shown to be an important adjunct to amphotericin B as well as an agent for primary treatment. In contrast to amphotericin B the drug is given orally and its side-effects are minimal. These include a mild and apparently reversible anemia and elevation of the serum glutamic-oxalacetic transaminase. The recommended dosage is 150 mg per kg of body weight per day divided into six-hour intervals. The eradication rate is unknown, due to limited reports of the drug, but as a primary therapy it is probably somewhat less effective than amphotericin B. Combined use of the drugs has been cited in case reports, but it remains uncertain if the combination is more or less effective than either drug alone. As with amphotericin B, no practical end-point of treatment can be stated.

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The Use of AMICAR® in Subarachnoid Hemorrhage

THERE IS WIDESPREAD CONTROVERSY about the optimal time for surgical intervention after subarachnoid hemorrhage secondary to ruptured intracranial aneurysms. The risk of early recurrent bleeding is often a major consideration in determining the appropriate time for operation. Recently attempts have been made to tide the patient over the early critical days by using epsilon amino caproic acid (AMICAR®) to prevent clot lysis and recurrent hemorrhage.

Amicar is a synthetic monoamino carboxylic acid that is a competitive inhibitor of plasminogen (profibrinolysin) activators. It also inhibits plasmin (fibrinolysin) but to a lesser degree. Therefore it prevents formation of plasmin which is responsible for the destruction of fibrinogen, fibrin and other clotting components. Thus it inhibits the dissolution of clots, but conversely may exaggerate thrombotic tendencies.

It has been used to control hemorrhage during cardiac and thoracic operations, portacaval shunting, abruptio placentae and in the "fibrinolytic bleeding" associated with metastatic prostatic carcinoma and leukemia.

In preliminary neurosurgical reports, Mullan and Dawley noted recurrent hemorrhages in only two of thirty-five patients with subarachnoid bleeding who had received AMICAR. Norlen and